



Attorney's Docket No.: 11413-003001 / B2286US

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Marc Pignot et al.

Art Unit : 1645

Serial No. : 09/744,641

Examiner : Josephine Young

Filed : January 26, 2001

Title : NEW COFACTORS FOR METHYLTRANSFERASES

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, Elmar Weinhold, am a co-inventor with Marc Pignot, on the above-identified patent application.

2. I am an expert in the field of synthetic chemistry and was an expert at the time of the invention. At the time of the invention I was employed as a group leader at Max-Planck-Gesellschaft zur Foerderung der Wissenschaften, assignee of the above-referenced patent application. Presently I'm Professor of Organic Chemistry at the RWTH Aachen (Rheinisch-Westfälische Technische Hochschule; Technical University of Aachen). My resume is attached as documentation of my credentials.

3. I declare that one skilled in the art at the time of the invention using the teaching of the specification, including the exemplary protocols as set forth in Examples 1 and 2, pages 19 to 30 of specification, and variations thereof, and other protocols known in the art at the time of the invention, could have successfully made and used the claimed compounds using only routine screening of alternatives. In particular, one skilled in the art using the teaching of the specification and routine methods known in the art at the time of the invention could have

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8/6/03  
Jeanne Brown Rice  
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designed synthetic schemes to synthesize any member of the claimed genus of aziridine derivatives using only routine screening of alternatives.

4. I declare that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to determine if any synthesized specie could act as a co-factor for a SAM-dependent methyltransferase. In other words, it would have taken only routine screening to determine if an aziridine derivative of the invention could act as a co-factor for a SAM-dependent methyltransferase.

One skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to determine if a putative methyltransferase could have complexed with an aziridine derivative of the present invention. In other words, it would have taken only routine screening to determine if a methyltransferase could have complexed with an aziridine derivative of the present invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date: \_\_\_\_\_

07/24/03



Elmar Weinhold

***CURRICULUM VITAE***

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**Date of Birth:**

July 13, 1960

**Place of Birth:**

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**Positions/Education:**

since 06.00

**Professor of Organic Chemistry** at the Institut für Organische Chemie der RWTH Aachen, Germany.

07.93 – 05.00

**Group leader** at the Department of Physical Biochemistry (*Prof. Roger Goody*), Max-Planck-Institut für molekulare Physiologie, Dortmund, Germany.

**Habilitation in bioorganic chemistry** at the Fachbereich Chemie, Universität Dortmund, Germany, with the title:  
Synthesis of modified duplex oligodeoxynucleotides and cofactor analogues for structure-function studies of DNA methyltransferases.

03.93 – 05.93

**Visiting scientist** at the New England Biolabs, Inc., Beverly, MA, USA.

- 03.91 – 02.93      **Postdoc** at the Department of Chemistry, Harvard University, Cambridge, MA, USA.  
Postdoctoral fellow of the Deutsche Forschungsgemeinschaft in the laboratory of *Prof. Jeremy R. Knowles* with the project title: Binding studies of synthetic sialic acid derivatives and influenza A hemagglutinin
- 07.86 – 02.91      **Ph.D.** at the Laboratorium für Organische Chemie der ETH-Zürich, Switzerland.  
Ph.D. thesis in the group of *Prof. Steven Benner* with the title: Protein engineering: A method for understanding the relationship between structure and activity of alcohol dehydrogenase from yeast.
- 02.86 – 06.86      **Graduate Student** at the Department of Chemistry, Harvard University, Cambridge, MA, USA.
- 03.80 – 01.86      **Diploma in Chemistry** (very good) at the Freie Universität Berlin, Germany.  
Diploma thesis with *Prof. Johann Mulzer* in the field of asymmetric synthesis.

#### Peer-reviewed publications

26. A. David, N. Bleimling, C. Beuck, J.-M. Lehn, E. Weinhold, M.-P. Teulade-Fichou, "DNA mismatch-specific base flipping by a bisacridine macrocycle", *ChemBioChem*, submitted.
25. C. Bolm, D. Müller, C. Dalhoff, C. P. R. Hackenberger, E. Weinhold, "The stability of pseudopeptides bearing sulfoximines as chiral backbone modifying element towards proteinase K", *Biorg. Med. Chem. Lett.*, in press.
24. C. Beuck, I. Singh, A. Bhattacharya, W. Hecker, V. S. Parmar, O. Seitz, E. Weinhold, "Aromatic DNA-base surrogates confer high-affinity binding to a native base flipping DNA methyltransferase", *Angew. Chem.*, in press.
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15. B. Holz, E. Weinhold, "Higher binding affinity of duplex oligodeoxynucleotides containing 1,2-dideoxy-D-ribose to the *N*<sup>6</sup>-adenine DNA methyltransferase *M-TaqI* supports a base flipping mechanism", *Nucleosides & Nucleotides* **1999**, *18*, 1355–1358.
14. B. Holz, N. Dank, J. E. Eickhoff, G. Lipps, G. Krauss, E. Weinhold, "Identification of the binding site for the extrahelical target base in *N*<sup>6</sup>-adenine DNA methyltransferases by photo-cross-linking with duplex oligodeoxyribonucleotides containing 5-iodouracil at the target position", *J. Biol. Chem.* **1999**, *274*, 15066–15072.
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3. G. Pljevaljic, F. Schmidt, A. Peschlow, E. Weinhold, "Sequence-specific DNA labeling using methyltransferases" in *Methods in Molecular Biology: Bioconjugation Protocols* (Ed.: C. M. Niemeyer), Humana Press, NY, in press.
2. B. Holz, E. Weinhold, "Probes for DNA base flipping by DNA methyltransferases" in *Bioorganic Chemistry: Highlights and New Aspects* (Eds.: U. Diederichsen, T. K. Lindhorst, B. Westermann, L. Wessjohann), Wiley-VCH, Weinheim, **1999**, pp. 337–345.
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14. K. Goedecke, M. Pignot, R. S. Goody, A. J. Scheidig, E. Weinhold, "Crystal structure of the N6-adenine DNA methyltransferase M-TaqI in complex with DNA and a cofactor analogue", *Biol. Chem.* **2001**, *382*, S170.
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